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DEPARTMENT OF OCCUPATIONAL HEALTH

3P

August 17, 1964

Grants and Research Contracts
Code SC
Office of Space Sciences
National Aeronautics and Space Administration
Washington, D. C. 20546

Dear Sir:

This is the fourth quarterly progress report submitted in accordance with the requirements of NASA Contract NASr-169 covering the period 1 April 1964 through 30 June 1964.

Significant progress has been made in the accomplishment of the three tasks associated with the automatic chromosome analysis system.

1. Automatic Microscope. In order to define the specifications for the subcontractor who will develop the automatic microscope, we have investigated several problem areas. One of these is the electro-mechanical link. This link is involved in moving the microscope stage along the "X", "Y" and "Z" axis and automatic slide loading. A literature search has shown that micro-positioners are available that are capable of positioning to less than five microns. This would meet our requirements for the "X" and "Y" coordinates, but is probably not adequate for the "Z" coordinate. Calculations and experiments have shown that the depth of field for 1000X magnification is on the order of two microns or less. Although Bostrom[1] et al., have devised a simple technique for maintaining a coarse focus, the mechanical problem dealing with fine focus is still a difficult one. A solution to this problem should be in sight before any extensive work is carried out on the logic requirements.

Another problem is the logic requirements for mitotic cell identification focus, stage traverse, and mitotic cell size and centering decision. The amount of logic required to perform the above functions is completely unknown. The amount of logical circuits required may be such that it would make the automatic microscope economically impractical. In order to evaluate these

[1] Bostrom, R. C., Sawyer, H. S., and Tolles, W. E., "Instrumentation for Automatically Pre-screening Cytological Smears", Proceedings of the IRE, Volume 47, No. 11, November, 1959.

requirements we are considering three approaches: normal incoherent light microscopy, variable wavelength incoherent light microscopy and laser or coherent light microscopy. To summarize briefly: the incoherent light microscope can convey only amplitude information; however, the coherent light microscope can convey both amplitude and phase information. With amplitude and phase information the logic requirements may be greatly reduced. The variable wavelength incoherent light microscope may also greatly reduce the logic requirements.

In May we received from the Perkin-Elmer Company, engineering report number 7662, which is a proposal for a detailed design study of the automatic microscope problem that is to result in systems specifications and a design approach to all significant optical, mechanical, and electronical design problems associated with the construction of the prototype instrument.

This proposal was given detailed examination and a number of modifications were considered. Another meeting with Kendall Preston was planned for July, at which time the nature of modifications would be resolved.

2. Digital Scanner. We have completed the image dissector investigation and a literature search of mechanical and electrical flying spot scanners as applied to film scanners and microscopes. We also visited four sites in May and June that are using either flying spot scanners[1,2] or image dissectors[3,4] for similar applications. As it appears now, we will not use the image dissector since the cathode non-uniformity may be a significant problem for our application. Calculations have shown that its low sensitivity is also a significant problem, although this aspect can be overcome with proper design.

The calculation of the image dissector sensitivity has led us to change the design of our scanning technique and analog-to-digital converter. Our original design was based on a pre-set dwell time for each scan element. This technique gives a uniform gray scale accuracy and the ability to easily obtain more gray levels if the need arises. This, it seems, is the best design for accuracy and flexibility. It will allow us to use an image dissector if and when cathode non-uniformity can be overcome.

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[1]University of Pennsylvania, Dr. M. L. Mendelsohn.
[2]Bureau of Standards, Dr. George Moore.
[3]ITT Federal Laboratory, Mr. Robert Lawberg.
[4]MIT Lincoln Laboratory, Mr. Don Malpass, Mr. Richard Horewitz

At present, the flying spot scanners appear to suit our needs best. Both electrical and mechanical flying spot scanners have been investigated and to obtain our 1000 by 1000 matrix, the electrical device is very expensive. For this reason we will build a mechanical flying spot scanner. When the resolution requirements are better known and if an incoherent light microscope can be used we will reconsider the electrical flying spot scanner. The flying spot scanner will be used in a film scanner. The purpose of the film scanner is to obtain data necessary in determining focus and resolution as well as data for programming the chromosome analysis problem.

Progress has also been made in the assembly of the computer interface. The magnetic tape drive unit has been moved from the Computation Center to Children's Hospital and the three phase power necessary for its operation has been installed. We have completed the design and assembly of the memory power supply and have procured the logic power supply and a line voltage regulator. We have procured some of the logic modules and have set up a purchase agreement with the Digital Equipment Corporation for additional modules. At present we are lacking three vital items: a rack cabinet; a storage oscilloscope and a regular oscilloscope. When we receive these items we will be ready to start assembly of the interface logic.

3. Computer Program. In order to pursue this task further, it is now necessary to utilize actual images of chromosomes on film as the input to the computer. The assembly of the computer interface is necessary before much additional work can be carried out on the computer program. For this reason little effort has been expended on this task in this report period.

4. Future Plans. The first major task is to seek solutions of the many automatic microscope problems. This will be approached in two ways: first, by subcontracting all or, at least, the major part of the design and development of a coherent light microscope, and second, by computer simulation of the problems associated with mitotic cell recognition using only incoherent light information.

The second major task is to build a film scanner. This scanner will be used to obtain data necessary to determine focus, gray scale and resolution requirements for the automatic microscope. The device will also be used to collect input data for computer simulation of microscope problems. The other purpose of the scanner will be its use in the development of the computer program to perform chromosome analyses. Since all of these functions require computer time, a priority rating may have to be assigned in the future.

Respectfully submitted,

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Professor of
Radiation Health

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